

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of : Attorney Docket No. 2004_1542A
Alan M. SAWYER et al. : **Confirmation No. 9045**
Serial No. 10/511,148 : Group Art Unit 1643
Filed December 2, 2004 : Examiner Hong Sang
METHOD FOR PRODUCING : **Mail Stop: AMENDMENT**
MONOCLONAL ANTIBODIES

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Dr. Thomas Joos, the undersigned, a citizen of Germany, residing at , Eichhaldenstrasse 55 in Tuebingen, Germany, do hereby declare:

1. That I graduated from the Eberhard Karls Universität Tübingen with a degree in Biochemistry.
2. PhD in Biology (Dr. rer. nat) at the Max Planck Institute of Developmental Biology, Department of Cell biology, Prof. P. Hausen: "Integrin- α 5 during early embryogenesis of *Xenopus laevis*"
3. Scientific Advisory "Biochipnet" (www.biochipnet.de):
At the NMI, Reutlingen, Germany, I was initiating "The BioChipNet database" in the year 2000. The BioChipNet database" is a comprehensive and searchable information platform on microarrays and related fields such as microfluidics and bioinformatics.

related references:

Joos T, Bachmann J. Protein microarrays: potentials and limitations. Front Biosci. 2009 Jan 1;14:4376-85.

Hartmann M, Roeraade J, Stoll D, Templin MF, Joos TO. Protein microarrays for diagnostic assays. Anal Bioanal Chem. 2009 Mar;393(5):1407-16.

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Poetz O., Schwenk, J.M., Kramer S., Stoll D., Templin M.F. and Joos T.O. (2005). Protein microarrays: catching the proteome. *Mechanisms of Ageing and Development*. 126 (1), 161-170

Joos T.O., (2004) Protein arrays: methods and protocols *Expert Rev. Proteomics* 1(3), 261-262

Templin M.F, Stoll D., Bachmann J., and Joos T.O. (2004) Protein microarrays and multiplexed sandwich immunoassays: what beats the beads? *Comb Chem High Throughput Screen*. 7(3), 223-229.

Stoll D., Bachmann J., Templin M.F., and Joos T.O. (2004) Microarray Technology: An Increasing Variety of Screening Tools for Proteomic Research. *TARGETS* 3(1), 24-31.

Templin M.F., Stoll D., Schwenk J.M., Potz O., Kramer S., and Joos T.O. (2003) Protein microarrays: Promising tools for proteomic research. *Proteomics* 3(11), 2155-2166

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Jutta Bachmann, Thomas Joos, Peter Welters, Alexander Bachor, Hugo Hämmerle. BioChipnet – an Internet Database for the BioChip Community. (2001) *BIOforum, International Life Sciences and Technology*, 4, 167

Thomas O. Joos, Dieter Stoll, and Markus F. Templin. Multiplexed Miniaturised Immunoassays. *Current Opinion in Chemical Biology* (2001) 2001, 6:76–80
Thomas O. Joos, Dieter Stoll, Monika Schrenk, Markus F. Templin. *Protein Microarray Technology*. (2001) *Screening*, 2 32 -34
Thomas O. Joos, Monika Schrenk, Peter Höpfl, Kerstin Kröger, Ushashi Chowdhury, Dieter Stoll, Dominik Schörner, Manfred Dürr, Klaus Herick, Steffen Rupp, Kai Sohn, Hugo Hämmerle. A Microarray ELISA for Autoimmune Diagnostics (2000), *ELECTROPHORESIS* 21, 2641 – 2650

Thus, as shown above, I am a person of skill in the art in the field of U.S. Application No. 10/511,148.

I have carefully examined the specification and claims of this application. Further, I have carefully examined the rejection in item 5 on pages 3-6 of the final Office Action with a mail date of June 23, 2009. It is my expert opinion and belief that a skilled artisan, based on the references cited in this rejection, would not arrive at the claimed invention. In particular, it is my expert opinion and belief that, based on the references cited in this rejection, a person of skill in the art in this field would not have realized that the claimed high-throughput method could be obtained with its inherent advantages for high-throughput production and screening of monoclonal antibodies against large numbers of antigens simultaneously.

In particular, I note that the claimed invention is directed towards a high-throughput method for providing a plurality of monoclonal antibodies each of which binds to a different candidate antigen comprising (1) introducing a plurality of purified candidate antigens into an animal or animals; (2) recovering antibody producing cells from said animal or animals, rendering the cells into single cell suspensions and generating immortalized cell lines from said single cell suspensions; (3) screening the supernatant of said immortalized cell lines against a protein chip on which purified candidate antigens are displayed; (4) and selecting monoclonal antibodies that bind to said candidate antigens.

I note that in order to arrive at the claimed invention from the teachings cited by the Examiner, a person of skill in the art would have to (1) substitute the homogenized cell extract of Chen with purified candidate antigens, (2) substitute the monoclonal antibodies of Chen on the chip with the purified antigens of the claimed invention and (3) replace the detection method of Chen, which comprises adding an antigen and a polyclonal antibody to the chip of Chen, with the streamline process of merely adding supernatant of the immortalized cell lines of the claimed invention.

I note that the Examiner utilizes the teachings of Rava to motivate a skilled artisan to substitute the monoclonal antibodies on the chip taught in Chen with a chip having purified antigens on the surface. However, a person of skill in the art, reading Rava would be confronted with a large number of options for probes on a peptide chip.

It is my expert opinion and belief that without the insight of the inventors, a person of skill in the art would not choose to display purified antigens on the surface of a chip in order to obtain a high-throughput method for producing a plurality of monoclonal antibodies.

I further note that Klessing, Poethke and Hu suggest immunizing animals with plurality of antigens. However, a skilled artisan would not be motivated to use a plurality of purified antigens in the method of Chen unless such skilled artisan realized the advantages of a high-throughput method for producing a plurality of monoclonal antibodies using a chip with purified antigens on its surface. It is my expert opinion and belief a person of skill in the art would not make such realization based on the cited references.

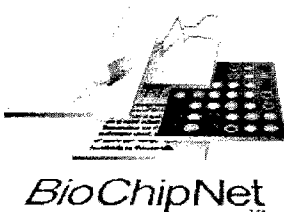
Thus, it is my expert opinion and belief that based on the references cited in the above-noted rejection, person of skill in the art would not have realized the claimed invention.

Finally, I note that as someone of skill in the art, the claimed invention has considerable advantages over the methods of producing monoclonal antibodies that are currently available. Such advance in monoclonal antibody production is highly significant as it dramatically reduces cost and time periods associated with such antibody production. Given such enormous advantages of the claimed invention, it is further my expert opinion and belief that if such method was obvious to a skilled artisan based on the references cited by the Examiner, such method would have been obtained at an earlier date by another inventor.

I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

18. Dec. 2009
Date

Thomas Joas
Signature of Declarant



NMI

Angewandte F&E

**Dr. Thomas Joos, Head Biochemistry Department,
NMI Natural and Medical Sciences Institute at the University of Tübingen,
Markwiesenstr. 55, 72770 Reutlingen, Germany**

Dr. Thomas Joos is head of the Biochemistry Department of the NMI Natural and Medical Sciences Institute at the University of Tübingen. Dr. Joos has been with the NMI since 1998, where he has been responsible for protein microarray technology for proteomic research and diagnostics. Recently, Dr. Joos joined in a part time position (25%) EDI GmbH, Reutlingen, Germany, the german subsidiary of Rules Based Medicine Inc., Austin, TX, USA to manage public granted projects.

Prior to joining the NMI, Dr. Joos did his postdoctoral research in the laboratory of Prof. Peter Hausen at the Max-Planck-Institute of Developmental Biology, Department of Cell biology, researching cell-cell and cell-matrix interaction during early embryogenesis of *Xenopus laevis*. Dr. Joos studied Biochemistry at the University of Tübingen. He received his Ph.D. degree in 1985 on integrin- $\alpha 5$ during early embryogenesis of *Xenopus laevis*.

Dr. Joos is a scientific advisor of BioChipNet (www.biochipnet.de), a member of the editorial board of Drug Discovery Today, Proteomics, Genomics Insights, Molecular Biotechnology and Expert Review of Proteomics. He is a member of the scientific advisory board of the "Plasma Proteome Institute" Washington, DC, USA and of the SAB of the "AlbaNova VINN Excellence Centre for Protein Technology (ProNova)" at the Royal Institute of Technology, Stockholm, Sweden. Dr. Joos is a member of the SAB of Luminex Corporation, Austin, TX, USA, of Rules Based Medicine Inc., Austin, TX, USA, and of Wellspring Clinical Lab, Inc. Altamonte Springs, FL, USA. Dr. Joos is an invited speaker, advisor and chairman at major international biochip conferences. Dr. Joos is a world leading expert and opinion leader within the field of protein microarray technology.